L14: Entry 1 of 1 File: DWPI May 3, 1990

DERWENT-ACC-NO: 1990-163991
DERWENT-WEEK: 200031

TITLE: New O-3-amino-2-hydroxypropyl hydroxamic acid halide derivs. - used for treating diabetic angiopathy, with selective action on altered beta receptors

INVENTOR: ABRAHAM, L; ALMASY, A ; BALAZS, B ; BLASKO, G ; BOROSS, M ; GACHALYI, B ; NAGY, P L ; NEMETH, G ; SZILBEREKY, J ; ZSILA, G ; ALMASI, A ; LITERATI NAGY, P ; NEMET, G ; SZILA, G ; LITERATI, N P ; BACHALYT, B ; BLASEO, G ; ZSILLA, G ; BALAAZS, B

PATENT-ASSIGNEE:

ASSIGNEE	CODE
BIOREX KUTATO FEJLESZTO KFT	BIORN
BIOPHARM KUTATO & FEJLESZTOE KFT	BIOPN
BIOREX KUTATO FEJLESZTOE KFT	BIORN
BIOREX KUTATO-FEJLESZTO KFT	BIORN
NAGY P L	NAGYI
BIOREX KUTATO FEILESTE KFT	BIORN

PRIORITY-DATA: 1988HU-0005405 (October 20, 1988), 1989WO-HU00048 (October 19, 1989), 1989JP-0510821 (October 19, 1989), 1992US-0906402 (July 1, 1992)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 9004584 A	May 3, 1990		000	
KR 154117 B1	December 1, 1998		000	C07C251/58
PT 92041 A	April 30, 1990		000	
CA 2000830 A	April 20, 1990		000	
AU 8944186 A	May 14, 1990		000	
FI 9003075 A	June 19, 1990		000	
NO 9002703 A	September 3, 1990		000	
DK 9001497 A	June 19, 1990		000	
HU 54110 T	January 28, 1991		000	
EP 417210 A	March 20, 1991		000	
ES 2020030 A	July 16, 1991		000	

☐	JP 03502931 W	July 4, 1991		000	
☐	US 5147879 A	September 15, 1992		006	A61K031/445
☐	HU 207988 B	July 28, 1993		000	C07C259/02
☐	EP 417210 B1	March 9, 1994	E	020	C07C251/58
☐	US 5296606 A	March 22, 1994		009	C07D211/04
☐	DE 68913737 E	April 14, 1994		000	C07C251/58
☐	IL 92000 A	June 24, 1994		000	C07C259/02
☐	US 5328906 A	July 12, 1994		011	A61K031/47
☐	FI 93214 B	November 30, 1994		000	C07D295/088
☐	IE 65113 B	October 4, 1995		000	C07C249/12
☐	NO 178148 B	October 23, 1995		000	C07D295/088
☐	JP 96019078 B2	February 28, 1996		010	C07C259/02
☐	CA 2000830 C	September 16, 1997		000	C07C257/02
☐	RU 2093508 C1	October 20, 1997		011	C07C251/58
☐	PH 28843 A	April 5, 1995		000	C07D295/14

DESIGNATED-STATES: AU DK FI JP KR NO SU US AT BE CH DE FR GB IT LU NL SE AT BE CH DE FR GB IT LI LU NL SE AT BE CH DE FR GB IT LI LU NL SE

CITED-DOCUMENTS:AT 355554; US 4308399

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
KR 154117B1	October 19, 1989	1989WO-HU00048	
KR 154117B1	June 19, 1990	1990KR-0701346	
EP 417210A	October 19, 1989	1989EP-0911590	
ES 2020030A	October 20, 1989	1989ES-0003542	
JP 03502931W	October 19, 1989	1989JP-0510821	
US 5147879A	October 19, 1989	1989WO-HU00048	
US 5147879A	June 28, 1990	1990US-0499318	
US 5147879A		WO 9004584	Based on
HU 207988B	October 20, 1988	1988HU-0005405	
HU 207988B		HU 54110	Previous Publ.
EP 417210B1	October 19, 1989	1989EP-0911590	
EP 417210B1	October 19, 1989	1989WO-HU00048	
EP 417210B1		WO 9004584	Based on
US 5296606A	October 19, 1989	1989WO-HU00048	Div ex
US 5296606A	June 28, 1990	1990US-0499318	Div ex
US 5296606A	July 1, 1992	1992US-0906402	
US 5296606A		US 5147879	Div ex
DE 68913737E	October 19, 1989	1989DE-0613737	
DE 68913737E	October 19, 1989	1989EP-0911590	
DE 68913737E	October 19, 1989	1989WO-HU00048	

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DE 68913737E		EP 417210	Based on
DE 68913737E		WO 9004584	Based on
IL 92000A	October 16, 1989	1989IL-0092000	
US 5328906A	June 28, 1990	1990US-0499318	Div ex
US 5328906A	July 1, 1992	1992US-0906402	CIP of
US 5328906A	June 7, 1993	1993US-0072765	
US 5328906A		US 5147879	Div ex
US 5328906A		US 5296606	CIP of
FI 93214B	October 19, 1989	1989WO-HU00048	
FI 93214B	June 19, 1990	1990FI-0003075	
FI 93214B		FI 9003075	Previous Publ.
IE 65113B	October 19, 1989	1989IE-0003364	
NO 178148B	October 19, 1989	1989WO-HU00048	
NO 178148B	June 18, 1990	1990NO-0002703	
NO 178148B		NO 9002703	Previous Publ.
JP 96019078B2	October 19, 1989	1989JP-0510821	
JP 96019078B2	October 19, 1989	1989WO-HU00048	
JP 96019078B2		JP 3502931	Based on
JP 96019078B2		WO 9004584	Based on
CA 2000830C	October 17, 1989	1989CA-2000830	
RU 2093508C1	October 19, 1989	1989SU-4830570	
RU 2093508C1	October 19, 1989	1989WO-HU00048	
PH 28843A	October 18, 1989	1989PH-0039379	

E INT-CL (IPC): A61K 31/13; A61K 31/135; A61K 31/15; A61K 31/21; A61K 31/395; A61K 31/405; A61K 31/435; A61K 31/44; A61K 31/445; A61K 31/47; C07C 219/06; C07C 249/12; C07C 251/58; C07C 257/02; C07C 259/02; C07C 259/04; C07C 295/12; C07D 207/00; C07D 209/04; C07D 211/00; C07D 211/04; C07D 211/60; C07D 213/04; C07D 213/44; C07D 213/54; C07D 213/78; C07D 215/00; C07D 223/00; C07D 225/00; C07D 231/00; C07D 237/00; C07D 243/00; C07D 295/00; C07D 295/08; C07D 295/088; C07D 295/12; C07D 295/121; C07D 295/14; C07D 295/15; C07D 401/12; C07D 413/12; C07D 450/00; C07D 471/06; A61K 31/15

ABSTRACTED-PUB-NO: EP 417210B
BASIC-ABSTRACT:

Hydroxamic acid halides of formula (I) and their salts are new: In (I), X = F, Cl, Br or iodo; R1 = H or 1-5C alkyl; R2 = 1-5C alkyl, 5-7C cycloalkyl or phenyl (opt. substd. by OH), or NR1R2 is a 5-8 membered ring, opt. contg. an additional N and/or O atom and opt. fused to a benzene ring; R3 = H, phenyl, naphthyl or pyridyl, opt. substd. by 1 or more halo or alkoxy; R4 and R5 = H or phenyl; m and n = 0-2.

Also new are the intermediates of formula (VIII).

USE/ADVANTAGE - (I) are useful for treating diabetic angiopathy, esp. retinopathy and nephropathy. They have a selective beta-blocking action on receptors which has been altered as a result of diabetes but no significant effect on receptors in healthy blood vessels.
ABSTRACTED-PUB-NO:

US 5147879A
EQUIVALENT-ABSTRACTS:

Hydroximic acid derivatives of the general formula (I) and the salts thereof, wherein X is halo, such as fluoro, chloro, bromo and iodo, R1 is hydrogen or C1-5 alkyl, R2 is C1-5 alkyl, C5-7 cycloalkyl or phenyl optionally substituted with hydroxy, or R1 and R2, when taken together with the adjacent nitrogen, form a 5 to 8 membered ring optionally containing additional nitrogen and/or oxygen atom, which ring may also be condensed with a benzene ring, R2 is hydrogen, phenyl, naphthyl or pyridyl optionally substituted with one or more halo or alkoxy, R4 is hydrogen or phenyl, R5 is hydrogen or phenyl, m is 0, 1 or 2 and n is 0, 1 or 2.

Hydroxamic acid derivs of formula R3-(CHCR4))m-(CH(R5).)n -C(X)=N-OCH2-CHCOH) -CH2-NR1RR2 (I) and their salts are new, where X is F, Cl, Br or I; R1 is H or 1-5C alkyl; R2 is 1-5C alkyl or 5-7C cycloalkyl; or NR1R2 form a 5-8 membered satd. ring; R3 is H, phenyl, naphthyl, or pyridyl opt. substd. by one or more halo and/or alkoxy; R4 and R5 are independently H or Ph; m and n are independently 0-2. USE/ADVANTAGE - The cpds. do not influence (or only slightly) the adrenergic reactions of healthy blood vessels, but show a strong effect on the adrenergic receptors deformed by diabetes mellitus. This effect appears as a selective beta-blocking effect, and (I) are useful for treating diabetic angiopathy, esp. diabetic retinopathy and diabetic nephropathy. They are ineffective on non-diabetic persons.

US 5296606A

Derivs. of O-(3-amino-2-hydroxypropyl)-hydroximic acid halides of formula (VIII) are new. In the formula, X is halo; R1 and R2 together with attached N form 5- or 8-membered satd. ring; R3 is H, Ph, naphthyl, or pyridyl opt. substd. by one or more halo or alkoxy; R4 and R5 are H or Ph; m and n are 0-2.

USE - Treatment of diabetic angiopathy., These cpds. are special selective beta blockers which convert alpha adrenoreceptors which have been modulated into beta receptors by diabetes mellitus back into normal alpha adrenoreceptors, so correcting vascular deformations. Applicable to all forms of diabetic micro- and macro-angiopathy, esp. diabetic retinopathy and nephropathy.

WO 9004584A

CHOSEN-DRAWING: Dwg.0/0 Dwg.0/0 Dwg.0/0 Dwg.0/0

TITLE-TERMS: NEW AMINO HYDROXYPROPYL HYDROXAMIC ACID HALIDE DERIVATIVE TREAT DIABETES SELECT ACTION ALTER BETA RECEPTOR

DERWENT-CLASS: B03 B05

CPI-CODES: B07-H03; B10-A18; B12-E06B; B12-G03; B12-H05; B12-L04;

CHEMICAL-CODES:

Chemical Indexing M2 *01*
Fragmentation Code
C009 C017 C035 C053 D010 D020 D040 F010 F011 F012
F013 F014 F020 F021 F431 F433 G001 G002 G010 G011
G012 G013 G019 G020 G021 G030 G040 G050 G100 G111
G112 G113 G221 G553 G563 H1 H102 H103 H141 H161
H181 H201 H4 H401 H402 H441 H481 H521 H522 H523
H541 H542 H543 H601 H602 H603 H604 H608 H609 H621
H622 H623 H641 H642 H643 H8 K0 K8 K840 L5
L512 M121 M122 M123 M129 M132 M135 M139 M150 M210

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M211 M212 M213 M214 M215 M216 M220 M221 M222 M231
M232 M233 M272 M273 M280 M281 M282 M283 M311 M312
M313 M314 M321 M322 M332 M342 M343 M344 M372 M383
M391 M412 M413 M414 M510 M511 M520 M521 M522 M530
M531 M532 M533 M540 M541 M640 M650 M710 M903 M904
P512 P922
Markush Compounds
199021-38501-N
Registry Numbers
1327U 0502U

Chemical Indexing M2 *02*
Fragmentation Code
C009 C017 C035 C053 D010 D020 D040 F010 F011 F012
F013 F014 F020 F021 F431 F433 G001 G002 G010 G011
G012 G013 G019 G020 G021 G030 G040 G050 G100 G111
G112 G113 G221 G553 G563 H1 H102 H103 H141 H161
H181 H201 H401 H441 H521 H522 H523 H541 H542 H543
H6 H601 H602 H603 H604 H608 H609 H621 H622 H623
H641 H642 H643 H682 K0 K8 K840 L5 L512 M121
M122 M123 M129 M132 M135 M139 M150 M210 M211 M212
M213 M214 M215 M216 M220 M221 M222 M231 M232 M233
M272 M273 M280 M281 M282 M283 M311 M312 M313 M314
M321 M322 M332 M342 M343 M344 M362 M372 M391 M412
M413 M414 M510 M511 M520 M521 M522 M530 M531 M532
M533 M540 M541 M710 M903 M904
Markush Compounds
199021-38502-N
Registry Numbers
1327U 0502U

SECONDARY-ACC-NO:
CPI Secondary Accession Numbers: C1994-103345

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